well known to most of you that life insurance companies at the present time refuse absolutely to accept as risks any persons who suffer from chronic discharge of the middle ear. An attempt should certainly be made to cure permanently all cases of chronic otorrhœa. Local measures—removal of the necrosed ossicles and of other known methods—should be made use of before resorting to external operation.

INFECTION OF THE RECTUM, WITH SECONDARY INFECTION OF THE LIVER, CAUSED BY THE BACILLUS INFLUENZÆ SIMILIS.[1]

By W. Ophüls, M.D.

(From the Pathological Laboratory of Cooper Medical College, San Francisco, Cal.)

The following case of what appears to be an infection with a bacterium belonging to the group of the influenza bacillus seems interesting enough to be put on record. I am greatly indebted to Dr. J. O. Hirschfelder for his allowing me to make use of the clinical history of the case in this paper.

J. B., aged thirty-six years, single, Austrian, laborer in mine, admitted November 29, 1900. Service of Dr. J. O. Hirschfelder. On admission: temperature 102°, pulse 100, respiration 48. Patient complains of severe chills, cold on chest, cough, and general malaise. No diseases of childhood. Father died of smallpox, mother of unknown cause; one brother alive and well; denies venereal history; drinks moderately and smokes excessively; has never been sick before, except with severe cold.

Present trouble came on eight days ago. On coming from Angel's Camp to Stockton he took a severe chill; was compelled to lay off for four or five days in Stockton. Then came to San Francisco; was in bed five days, while in Stockton most of the time. Arriving in San Francisco he went to the Receiving Hospital, and remained overnight. Was brought to the City and County Hospital November 28, 1900. Complains now (November 29th) of chills, followed by sweats, cough, expectoration of blood and mucus, sore-throat, headache, loss of appetite, diarrhœa for the last week, and jaundice.

Physical Examination (Dr. Hirschfelder). Patient well developed, fat, markedly icteric; head, no peculiarity; pupils equal, react to light; no scar in pharynx; gums normal; neck, nothing abnormal; cervical glands slightly enlarged; thorax well developed, deep, broad. Right side moves less than left. Tongue slightly coated. Flatness of right lower lobe. Bronchial respiration and râles of varying size. Sputum brownish-red, mucous. Area of cardiac dulness: third rib, left sternal border, fifth space, 2 cm. left of mammillary line. Tones clear, marked accentuation of second pulmonic sound. Abdomen distended; region of stomach sensitive; no tumor palpable; liver, 13 cm. in diameter;

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[1] Read at the Thirty-first Annual Session of the Medical Society of the State of California.

consistency somewhat increased. In region of gall-bladder smooth, round mass felt, not sensitive. Spleen extends to anterior axillary line, not palpable. Right inguinal hernia, easily replaced. Inguinal glands slightly enlarged. No scars on penis.

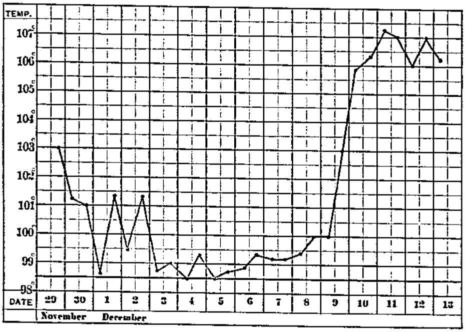
November 29th. Patient decidedly icteric; had severe nose bleeding. Pulse 82, full, regular.

30*th.* Nose bled twice during the day.

December 1st. Nose bled twice this morning; sweat some during the night; tongue coated with brownish-gray coating. Dulness in right lower lobe of lung continues; liver, 11½ cm. in diameter; abdomen somewhat distended. Region of gall-bladder sensitive; spleen not enlarged.

3*d.* Urine: specific gravity 1016; reaction acid; albumin, trace; sugar, diazo reaction, indican negative. Bile pigment present.

5*th.* Patient decidedly more icteric.



10*th.* Patient somewhat more icteric. Pulse 80, full. No dulness of the lungs, vesicular respiratory murmur. Area of cardiac dulness: lower border of third rib, left sternal border, sixth interspace, 2 cm. to left of mammillary line; tones clear; liver 9 cm. in diameter, consistency somewhat increased; gall-bladder not palpable; spleen not enlarged; abdomen not distended.

11*th.* Pulse 106, respiration 46. Tongue coated with grayish fur; right pupil somewhat larger than left; no dulness of lungs; both tonsils somewhat reddened; on right tonsil yellowish deposits.

12*th.* Pulse 108, respiration 48. Slight tonsillitis; very small patch on right tonsil; lungs normal; numerous râles are heard over anterior portion of chest; systolic murmur at apex and pulmonic valves; tones at apex indistinct; liver 10 cm. in diameter; spleen not enlarged; abdomen somewhat distended with gas; region of gall-bladder sensitive; gall-bladder palpable; slight ileocæcal gurgle; tongue moist, coated.

13*th.* Patient decidedly more icteric. Pulse 116, fairly strong; tongue coated; dulness of right lower lobe of lungs; bronchial breathing; a few râles; liver, 16½ cm. in mammillary line; to the right of median line, 13½ cm.; consistency increased; markedly sensitive; gall-bladder palpable, painful; spleen enlarged, not palpable. Patient is so dyspnœic that character of cardiac tones cannot be determined.

Blood: White corpuscles, 7200 in c.mm.; polymorphonuclear leucocytes, 80 per cent.; small mononuclear leucocytes, 14 per cent.; large mononuclear leucocytes, 5⅔ per cent.; eosinophiles, ⅓ per cent.

Post-mortem Record. J. B., aged thirty-six years, laborer, died December 14, 1900, 8 A.M.

Autopsy, December 14th, 10.30 A.M. Strongly built, muscular, moderately well-nourished man. Shoulders slightly stooping. Slight enlargement of the femoral lymphatic glands. Slight cyanosis of lower face and neck. Skin and mucous membranes are bright yellow. Abdomen a little distended; marked rigor mortis. Liver projects two finger-breadths below free margin of ribs in mammillary line. The lower end of the omentum is fastened to the hernial sac of a small inguinal hernia on the right side. Lower border of stomach at umbilicus. A few drops of clear, yellow fluid in rectovesical pouch. Diaphragm at the fourth rib on both sides. Thorax broad, symmetric. Stringy, easily broken adhesions in the lower part of left pleura. The larger part of the right pleural sac obliterated by similar adhesions. About 100 cm. of clear, dark, yellow fluid in pericardium. Both sides of heart distended and filled with dark fluid blood. Right ventricle averages 3, left 12 mm. in thickness. Valves, aorta, coronary arteries normal, except for bright-yellow discoloration of intima and endocardium. Heart muscle normal.

Left pleura, many small hemorrhages in adhesions. Bronchi on left side empty, cyanotic. Lower lobe and posterior part of upper lobe of left lung contain little air and much blood. Anterior portion of lung normal. Right lower lobe firmly attached to the upper surface of the diaphragm. Numerous small hemorrhages in adhesions. About in middle of lateral surface of upper right lobe there is a bright yellow, dull spot in pleura, measuring about 2 cm. in diameter, and surrounded by a hyperæmic zone. The pleura in the neighborhood is a little opaque and rough on surface. Beneath the discolored pleura there is a necrotic area of light-yellow color extending about 1 cm. into the pulmonary tissue. Around it is a hyperæmic zone. The bronchial tubes on the right side contain a little bloody mucus. In one of the large bronchi of the lower lobe one finds enveloped, in a little bloody mucus, a hard, stony, irregular, grayish-white, non-obstructing concretion, 7 x 5 x 3 mm. in size (quite apparently a concretion from the tonsils or the ducts of one of the salivary glands that was aspirated shortly before death).

The mucous membrane of the bronchi on the right side is anæmic, intensely icteric, otherwise normal, even in neighborhood of foreign body. The right lower lobe of lung contains little air. Rest of lung normal. Spleen, 15½ x 8½ x 4½ cm. A few just visible white thickenings of capsule on convexity. The organ is hard, cut surface smooth, dark red. Markings distinct. Adrenals normal. Left kidney: capsule a little adherent; size, 14½ x 6½ x 3 cm. Consistency soft. A considerable amount of fatty tissue around renal pelvis. Cortex appears a little cloudy. Right kidney same as left. Appendix normal. Right testicle: slight thickening of the outer layer of the tunica vaginalis. Testis itself normal. Bladder contracted, contains a few drops of dark-yellow urine. Prostate a little large. Seminal vesicles normal. Rectum empty. Just above anus the mucous membrane shows some thick hyperæmic longitudinal folds, which are partly covered with brown sloughs. On incision two small abscess cavities are found in submucosa, near the sloughs on surface. Pelvic veins contain fluid venous blood, no macroscopic thrombi. Contents of duodenum strongly acid, not bile-stained. There is a good deal of mucus in them. Similar contents in stomach. On pressure a little orange-colored bile is discharged from bile duct. The ducts themselves are not obstructed, and are of normal size and appearance. Gall-bladder small; wall œdematous. Portal vein contains a little dark fluid. Hepatic artery normal. Stomach greatly distended. Mucous membrane in large folds, swollen, cloudy. Pancreas normal. Vena cava inferior, normal. Liver: surface shows a large number of bright yellow spots of size of millet-seed, most of them arranged in groups of twenty or more. They are surrounded by hyperæmic zones. Similar areas are found scattered all over cut surface. The small branches of the hepatic vein in their surroundings contain soft yellowish-gray thrombi. In the comparatively normal parts of the liver the lobuli show dark greenish-brown centres and light yellowish-brown peripheries. No thrombi in branches of portal vein. Slight opacity of the peritoneal covering of the right lobe of the liver. Jejunum distended, mucous membrane swollen, cloudy. Ileum, colon, appendix normal, contents moderately bile-stained. Sigmoid flexure shows slight irregular hyperæmic swellings of mucous membrane. It is covered with thick, viscid mucus. Slight enlargement of the thyroid. Rest of the organs of neck normal.

Diagnosis. Proctitis, with sloughing and abscess formation in submucosa; multiple metastatic abscesses of liver; septic thrombosis in hepatic veins, septic infarction of lung; gastro-enteritis; green icterus of liver; general icterus; pleuritic adhesions on both sides with hemorrhages in them; slight chronic and acute parenchymatous nephritis; enlargement of the thyroid; inflammatory enlargement of the spleen.

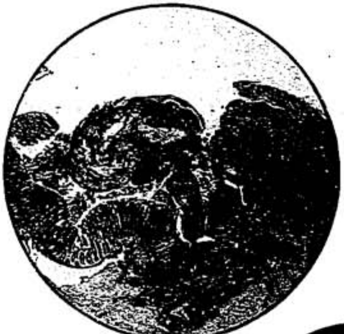
The result of the microscopical examination is the following:

Rectum. (Figs. 1 and 2.) In a number of places the mucous membrane and also part of the submucosa are destroyed. These small but deep defects are filled in and covered with old blood clots. The defects are surrounded by a thin layer of necrotic tissue, then follow layers of tissue which are very hyperæmic, full of small hemorrhages, and moderately infiltrated with lymphocytes and polymorphonuclear leucocytes. The connective tissue cells in these areas are large and seem to be increased in number. Many of them are full of minute fat droplets. There also seems to be some increase in the connective tissue fibrils.

The larger portion of the mucous membrane has normal structure and is covered with a thick layer of mucus. Many minute bacteria in irregular heaps in lower parts of blood clot and in tissue around defect. In Fig. 2 there is a small vein at the edge of which there are two large heaps of these bacteria.

Liver. (See Figs. 3 and 4.) The centres of the liver lobules show some stagnation hyperæmia, slight thickening of central veins, icteric pigmentation and stagnation of bile in bile capillaries. Many of the liver cells in centres of lobules are small and full of fat droplets. There are very many moderately large irregular areas in which the hepatic tissue is completely necrotic. In the necrotic material and in the liver cells

FIG. 1.



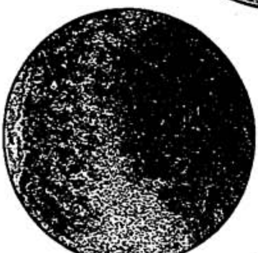


FIG. 3.

FIG. 4.

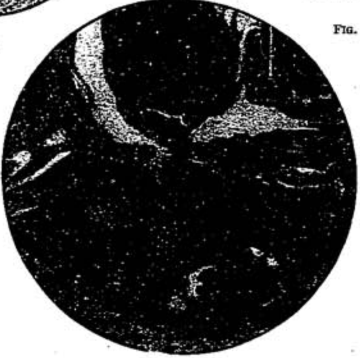


FIG. 2.

in surroundings of necroses there are some minute fat droplets. The necrotic material appears finely granular under the microscope. In the middle of some of the necrotic areas there is evidence of beginning liquefaction. The necrotic layers are surrounded by a cellular layer which consists largely of epithelioid cells with some lymphocytes and polymorphonuclear leucocytes. The cells near the necrotic material show pyknosis, caryorrhexis of their nuclei, and other signs of degeneration. Small branches of the hepatic vein in the neighborhood of these areas show fatty degeneration and necrosis of their wall. They are filled with thrombi that consist of fibrin, agglutinated blood platelets, and small heaps of fat granules. In the periphery of the necrotic areas and in the outer layers of the cellular tissue around them there are very many minute bacteria in thick, irregular heaps which in many places are situated in and follow the course of the capillaries. Similar bacteria are found in thrombi of the hepatic veins. No cocci to be found in sections stained with Gram's method. The bile ducts, unless secondarily involved, are normal.

Lung. Right upper lobe. Large, irregular necrosis. At apex of necrosis a branch of pulmonary artery, which is filled with a thrombus consisting of agglutinated blood platelets, leucocytes, and some epithelioid cells. In periphery of necrosis one finds the tissue infiltrated with the same cells as those which surround the necroses of the liver. The polymorphonuclear leucocytes are perhaps a little more numerous. The pleura over necrosis is partly necrotic, in other places hyperæmic, contains some small hemorrhages. It is covered with a thin layer of fibrin. Between fibrin and pleura in many places a row of swollen endothelial cells is plainly visible. Many minute bacteria in irregular heaps in periphery of necrosis and in embolus in branch of pulmonary artery. No cocci in sections stained with Weigert's modification of Gram's method. The comparatively normal parts of lung show marked thickening of septa, some œdema, a few hemorrhages, proliferation and desquamation of epithelial cells.

Jejunum: Lymphocytic infiltration of mucous membrane, many goblet cells in epithelium, much mucus on surface.

Stomach: Much mucus on surface, no structural changes.

Spleen: Hyaline degeneration of some of the arteries, hyperæmia, fatty degeneration of some of the cells of pulp.

Kidney: A few scattered small areas of chronic nephritis, icteric pigmentation, slight fatty degeneration in spots.

Thyroid: Follicles large, much colloid.

Tonsil: Fatty degeneration of germinal areas of follicles.

Testis: Normal.

Aorta: Slight irregular thickening of intima, with very marked fatty degeneration of connective tissue cells.

RESULT OF BACTERIOLOGICAL EXAMINATION. Cover-slips from abscesses in submucosa of rectum, necrosis of liver and lung show very many minute (largest diameter about 0.85μ) bacteria. They are mostly rod-shaped, but some of them are round, coccus-like. They stain hardly at all with methylene-blue, a little better, often somewhat irregularly, with carbol-fuchsin. Some show polar staining. Some appear as diplobacilli, or, again, as diplococci. In spots they form small clusters; here and there one finds a short thread. They do not stain with Gram's method.

Cultures taken at post-mortem (smear cultures on glycerin agar-agar).

Liver necrosis: two colonies of colon bacilli. Three minute dewdrop-like colonies of minute bacilli. One of the colonies is contaminated with streptococci.

Pus: Abscesses in submucosa of rectum; many colonies of colon bacilli; a few minute colonies like those in culture from necrosis of liver.

Contents of gall-bladder: Two colonies of colon bacilli. Three minute colonies like those in culture from necrosis of liver.

Lung, right lower lobe: Two colonies of staphylococcus pyogenes aureus; one colony of colon bacteria.

Spleen: No growth.

Kidney: One colony of staphylococci; two just visible colonies of streptococci.

The small bacilli that are found so abundantly in the sections and were isolated from necrosis of the liver and suppurating areas of rectum show the following cultural peculiarities:

Glycerin (6 per cent.) serum; no growth. Löffler's serum at 37° C.; after twenty-four hours just visible dewdrop-like colonies appear, which in two or three days grow to about 2 mm. in diameter and become a little more opaque. The centre of the colonies is a little raised and the margin slightly irregular.

Glycerin agar-agar, 37° C.; after twenty-four hours just visible dewdrop-like colonies appear, which later enlarge a little but not very much. They always remain transparent, have slightly irregular margin, raised centre. Macroscopically, and also under the low power of the microscope, they cannot be differentiated from colonies of pneumococci or a delicate growth of streptococci.

Sugar agar-agar; slight granular growth along track of needle; no fermentation.

Beef-tea remains clear; after a few days a little, finely granular sediment appears.

Milk[1] slowly acidified, not coagulated.

Potato: No growth.

Gelatin: No visible growth even after several weeks.

The growth on solid media is quite characteristic in that it forms a delicate grayish-white film that hangs together very tenaciously, so that in trying to remove some of it with the platinum needle, usually the whole colony or larger pieces of it come off. It is also impossible to obtain a good emulsion of them in water. The film, on being rubbed over the cover-slip, breaks up into small fragments, but one never achieves a separation of the individual germs. The just visible grayish-white flakes in the beef-tea are large clusters of bacteria, and show the same peculiarity. The bacteria are non-motile. They have about the same size as those found in the tissues, being, perhaps, slightly larger (about 1μ long). They stain badly with methylene-blue and even with carbol-thionin, well with dilute (1:5) carbol-fuchsin. For the periphery of the affected areas in sections and in fresh cultures the staining is more intense and more regular than in cover-slips from the tissues. They do not stain with Gram's method. In cultures not over twenty-four hours old an imperfect staining with the method may, however, be observed in such a way that some of them take the stain quite well, most of them not at all. It always seems to be the largest, best developed individuals that take the stain.

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[1] Could be tried only once on account of dying out of cultures.

Since, as I mentioned above, a true emulsion of them in water is not formed they always appear in cover-slips in the form of clusters in which the bacteria lie very close together, so much so that sometimes it is difficult to see the separating lines between them. They vary considerably in their shape; quite a good number of them appear to be perfectly spherical, others show diplococcus forms, but in all clusters one can find individuals that are decidedly rod-shaped. Threads were not found in the cultures. Here and there one sees individuals that are about twice the normal size, oval in shape, sometimes with slightly pointed ends. These larger forms take the stain very deeply. They are more numerous in old, pure cultures, in which the smaller forms stain hardly at all any more. Spores were not found in any of the cultures. On the culture media they often die out very quickly, but sometimes they remain alive for a considerable time. In one case I succeeded in obtaining a new culture from a culture on Löffler's serum that was about two months old. Naturally, I had to take a good deal of material, and the first growth was not very abundant.

In the sections the bacteria decolorize completely when the sections are treated with either Gram's method or Weigert's fibrin stain. The best results were obtained with sections stained in dilute (1:5) carbol-fuchsin and decolorized in alcohol. The bacteria in the periphery of the necrosis and in the tissues next to them have very much the same appearance as those in the pure cultures. Short threads, however, are quite frequently seen. Other bacteria could not be found; there were especially no cocci to be seen in sections from rectum, liver, and lungs, which were stained with Gram's method.

The following animal experiments were made December 20, 1900: Guinea-pig. Subcutaneous injections of about ½ c.cm. of a suspension of a culture on Löffler's serum in a little beef-tea. No swelling or redness observed at point of injection at any time. The guinea-pig was killed February 1, 1901. No lesions were found.

On December 20, 1900, another pig was inoculated intraperitoneally with same amount of same material. No symptoms of disease. Autopsy, February 1, 1901, negative.

January 18, 1901, rabbit. Intravenous injection of about 1 c.cm. of suspension from Löffler's serum culture. No local changes at point of injection. Autopsy, February 1, 1901, negative.

Further experiments could not be made on account of the dying out of the cultures.

Our case, then, is one of primary infection of the rectum with sloughing and ulceration, and secondary infection of the liver by way of the portal system. It is of some interest to note, in the first place, the absence of macroscopical septic thromboses in the hemorrhoidal plexus, and, secondly, the fact that although the infection was very low down in the rectum the infectious material was carried into the portal circulation.

It seems probable that the infection of the right lung is secondary to the septic thrombosis in the hepatic veins, an embolus having been carried away from the latter and lodged in one of the branches of the pulmonary artery.

The infectious agent I believe to be the bacterium which was found in such large numbers in the diseased tissues, and which was obtained in pure culture from the rectum, liver, and gall-bladder.

Animal experiments, it is true, have been so far perfectly negative, but they have not been on an extensive enough scale to prove the absence of pathogenic power in these bacteria for animals, and even if they should be perfectly innocuous to animals we should not be justified to draw the conclusion that this was also the case in regard to man. On the other hand, the relation of the bacteria in the tissues to the lesions is so eminently suggestive that to my mind it almost amounts to a positive proof of their etiological importance in this case. I am not inclined to attribute much importance to the few streptococci that were found in the liver and kidney, because they could not be demonstrated in the sections.

As far as the bacteria themselves are concerned, I have as yet not been able to identify them with any that have been described before. In consideration of their morphology—they being very minute, non-motile bacilli that do not form any spores, and also in consideration of the fact that they do not stain with Gram's method—they would appear to belong to the group of the influenza bacillus. From the influenza bacilli themselves they differ in growing on media that do not contain any hæmoglobin. They also differ in essential details from other members of this group that we find described in Kruse's article on bacilli in Flügge's micro-organisms (third edition, Leipzig, 1896, p. 435, viz.: B. pseudoinfluenza, R. Pfeiffer, *Zeitsch. f. Hygiene und Infectionskr.*, xiii.; B. cavernæ minutissimus, R. Pfeiffer und Beck, *Deutsche med. Woch.*, 1892; B. salivæ minutissimus, B. conjunctivitidis, Gaffky, *Arb. aus d. kais. Gesundheitsamt.*, iii.; B. pseudoconjunctivitidis, B. aeris minutissimus).

There seems to be a very close resemblance between our bacteria and the bacteria that have been described in the sputum in cases of whooping-cough by a number of authors in this country and in Europe. The identity or non-identity of the bacteria found by different authors in this disease has been a matter of much controversy. In reading the reports one certainly gets the impression that all of them have seen the same bacterium in the cover-slips prepared from the expectoration of the patients, whereas, there may be some doubt as to whether all succeeded in obtaining pure cultures of them.

Minor differences, which have played a very important rôle in this controversy, should, however, not be over-emphasized in view of the natural tendency to variation which we observe in all bacteria, especially when they are cultivated on artificial media.

The bacteria described in this paper morphologically correspond in all respects with the photomicrographs of Zusch and Vinceuze, whereas they differ a little in their appearance from the photomicrographs of Czaplewski, which, however, as he himself points out, may be due to his having photographed specimens from cultures that had grown on artificial media for long time.

As far as the cultures are concerned, the only essential difference between our bacterium and the ones described in whooping-cough (as far as one is able to judge from the conflicting reports of different authors) seems to be their failure to grow on gelatin, which, after all, may be due to the fact that the gelatin was kept at a rather lower temperature (about 15° C.) than is customary in most laboratories.

Provisionally, I should recommend to call the bacterium described in this paper B. influenzæ similis.

The interpretation of the clinical history is somewhat difficult. It seems certain that when first seen the patient was suffering and had been suffering from an attack of pneumonia, which cleared up within the usual time.

The icterus which accompanied the pneumonia was at the time looked upon as a catarrhal icterus, which was probably correct. At the autopsy there was evidence of an inflammation of the mucous membrane of the duodenum, but no other causes for an obstruction of the bile ducts could be discovered.

The abscesses of the liver show all the characteristics of a very recent infection. It seems very unlikely that they should be three weeks old, and, therefore, we cannot ascribe the jaundice that existed that long, to them, quite apart from the fact that none of them interfered with any of the large bile ducts.

The rectal ulceration seems to have developed insidiously without making any symptoms quite separately from the main disease, and it seems probable that the sudden rise of temperature on December 9th, five days before the patient died, marks the time when the secondary infection of the liver occurred.

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